(Review Article)

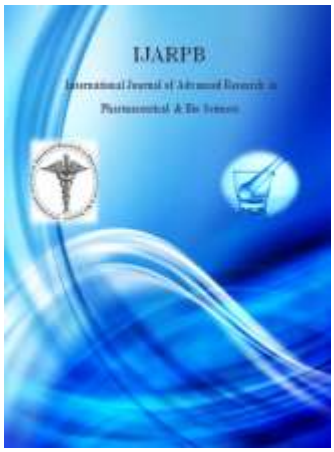
IJARPB
International Journal of Advanced Research in Pharmaceutical & Bio Sciences
(A peer reviewed International journal for Pharmaceutical and Bio Sciences)

Received on 05/01/2012; Revised on 19/01/2012; Accepted on 28/01/2012.

Allergy and Its Treatment - A Review

Bhadauria R S, Soan V, Arwa Rangeen*,

Lecturer, Shreenathji Institute of Pharmacy, Nathdwara (Raj.)



Corresponding Author:
Arwa Rangeen,
Lecturer,
Shreenathji Institute of Pharmacy, Nathdwara (Raj.)
Email:rangeen52@gmail.com

ABSTRACT

Allergy is characterized by local or systemic response to outside allergens such as dust, pollen or certain foods. Local symptoms are observed like allergic rhinitis, conjunctival, skin rasher and systemic symptoms like dyspnoea, bronchoconstriction, oedema, hypoknision, Coma and some time death also. Diagnosis of allergy is based on the medical history and physical examination. In case of diagnostic uncertainty, testing for specific antigens can be useful. Histamine is the main mediator for allergy. Histamine is present mostly within storage granules of mast cells, tissues mucosa, lungs, liver and placements. It is also present in blood, body secretions etc. Effect of Histamine is mediated through Histamine receptors H_1 H_2 and H_3. These receptors are situated in various parts.

KEY WORDS- Cetrizine Hydochloride, Levocetrizine Dihydrochloride, Desloratadine, Azelastine

(Review Article)

INTRODUCTION

The term allergy is used to describe a response, within the body, to a substance, which is not necessarily harmful in itself, but results in an immune response and a reaction that causes symptoms and disease in a predisposed person, which in turn can cause inconvenience, or a great deal of misery. When your body reacts to an outside substance, which it notes as a threat to its well-being is called an allergy. A misguided reaction to foreign substances by the immune system, the body system of defence against foreign invaders, particularly pathogens (the agents of infection). The allergic reaction is misguided in that these foreign substances are usually harmless[1]. The substances that trigger allergy are called allergen. Examples include pollens, dust mite, molds, danders, and certain foods. People prone to allergies are said to be allergic or atopic. Although allergies can develop at any age, the risk of developing allergies is genetic. This is how the immune system becomes misguided and primed to cause an allergic reaction when stimulated by an allergen[2].

The most common allergic conditions include hay fever (allergic rhinitis), asthma, allergic eyes (allergic conjunctivitis), allergic eczema, hives (urticaria), and allergic shock(also called anaphylaxis and anaphylactic shock). For a thumbnail sketch of each of these conditions: Hay fever (allergic rhinitis) is the most common of the allergic diseases and refers to seasonal nasal symptoms that are due to pollens. Year round or perennial allergic rhinitis is usually due to indoor allergens, such as dust mites or molds. Symptoms result from the inflammation of the tissues that line the inside of the nose (mucus lining or membranes) after allergens are inhaled. Adjacent areas, such as the ears, sinuses, and throat can also be involved. The most common symptoms include:

- Runny nose
- Stuffy nose
- Sneezing
- Nasal itching (rubbing)
- Itchy ears and throat
- Post nasal drip (throat clearing)

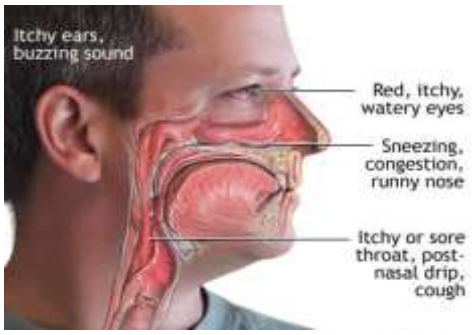


Fig:1 Symptoms of Allergy

In hay fever when the count of pollen is particularly high and we have two people walking on the streets. The individual whose immune system is balanced and does not react severely to any and every outside allergen will not even be aware of the high pollen count[3]. His eyes will not itch or water, and there will be no sneezing. But the other individual may react severely to the pollen and begin to sneeze because of the immune system's overreaction to this specific type of allergen. Perhaps the eyes will water. In extreme circumstances the person may have respiratory troubles and get choked if the body interprets the pollen as a dangerous invader to its system.

Fig:2 Symptoms of Asthma

(Review Article)

Asthma is a breathing problem that results from the inflammation and spasm of the lung's air passages (bronchial tubes) [4]. The inflammation causes a narrowing of the air passages, which limits the flow of air into and out of the lungs. Asthma is most often, but not always, related to allergies. Common symptoms include:

- Shortness of breath
- Wheezing
- Coughing
- Chest tightness

Fig:3 Allergic Eye

Allergic eyes (allergic conjunctivitis) is inflammation of the tissue layers (membranes) that cover the surface of the eyeball and the under surface of the eyelid. The inflammation occurs a result of an allergic reaction and features:

- Redness under the lids and of the eye overall
- Watery, itchy eyes
- Swelling of the membranes

Fig:4 Allergic Eczema

Allergic eczema is an allergic rash that is usually not caused by skin contact with an allergen and features the following symptoms:

- Itching, redness, and or dryness of the skin
- Rash around the eyes, in the elbow creases, and behind the knees, especially in adults

Fig:5 Symptoms of Urticaria

Hives (urticaria) are skin reactions that appear as itchy swellings and can occur on any part of the body. Hives can be caused by an allergic reaction, such as to a food or medication, but they also may occur in non-allergic people. Typical hive symptoms are:

- Raised red welts
- Intense itching

Fig:6 Symptoms of Anaphylaxis

Allergic shock (anaphylaxis or anaphylactic shock) is a life-threatening reaction that can affect a number of organs at the same time. It typically occurs when the allergen is eaten (for example, foods) or injected (for example, a bee sting) [5]. Allergic shock is caused by dilated and "leaky" blood vessels, which result in a drop in

blood pressure. Some or all of the following symptoms may occur:

- Hives or reddish discoloration of the skin
- Nasal congestion
- Swelling of the throat
- Stomach pain, nausea, vomiting
- Shortness of breath, wheezing
- Low blood pressure or shock

Catalyst and stirred at room temperature for four hour. The reaction mixture was poured into ice and filtered. The crude product so obtained was dried and recrystallized with methanol. Solvent system: Chloroform: Methanol (8:2).

History

The word "allergy" appeared in 1920 and derives from the adjective allergic which was first introduced. It derives from the German word '*allergisch*' (1906), which itself comes from the Greek *allos*: 'other' and *ergia*: 'action, efficacy.' The term atopy was introduced in 1923 and comes from the Greek letter '*a*' (prefix meaning without) and *'topos*': 'place' (without a place), to designate manifestations of allergic disorders, which could not be classified in the disease categories known at that time.

Causes of Allergy

Allergic reactions are caused by substances in the environment known as allergens. Almost anything can be an allergen for someone. Allergens contain protein, which is often regarded as a constituent of the food we eat. In fact it is an organic compound, containing hydrogen, oxygen and nitrogen, which form an important part of living organisms[6].

The body recognizes an intruder

The first time you breathe in ragweed pollen, your body identifies the pollen as a foreign, invading substance. Plasma cells, primarily located under mucus membranes, make large amounts of antibody against it. Your body can make a unique antibody for every type of pollen. In fact, it can make a unique antibody to every possible food ingredient, or anything else that comes from outside the body and is not "you." The type of antibody most commonly associated with allergic reactions is called Immunoglobulin E ("IgE"). The body has other ways to recognize and react to a substance; this example will focus on antibody reactions.

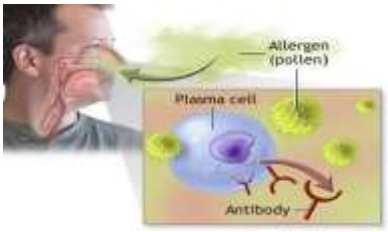


Fig:7 Body Recognizes as Intruder

The body gets ready

The IgE antibodies to ragweed pollen attach themselves to mast cells (which are located in tissue that lines the nose, bronchial tubes, as well as the gastrointestinal tract and the skin) and basophils (cells which circulate around in the bloodstream). The antibodies stick out from the surface of the mast cells and basophils, waiting. Your body is now "primed" and ready for any time in the future when ragweed pollen enters the body.

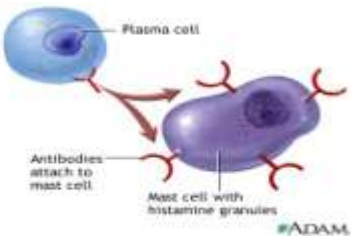


Fig:8 Antibody Reactions

The attack

The next time you breathe in ragweed pollen, the antibodies "grab" the pollen and send a signal down to the attached mast cells and basophils. Powerful chemicals are immediately released -- including histamine, heparin, and over 30 others. They cause the nearby tissue to become swollen and inflamed.

Fig:9 Attack of Allergen

The delayed response

Some people also will experience what is known as the "late phase" of an allergic reaction. This occurs because the chemicals associated with the reaction attract additional types of immune cells to the site of the allergic reaction, such as eosinophils, neutrophils, and lymphocytes. These cells, in turn, release chemicals which can actually cause tissue damage. The late phase can occur between 4 and 24 hours after exposure.

Substance That Causes Allergy

Allergens are everywhere -- in the air we breathe, in the food we eat, in the medicine and cosmetics we use, and in plants in our backyard. Here are the most common ones.

Airborne allergens

Airborne allergens are the hardest to avoid, particularly pollen. Inhaling an allergen is the most common way people are exposed. This explains why allergy to pollen (also referred to as "hay fever") affects about 40 million Americans, according to the American Academy of Allergy, Asthma, and Immunology. Read detailed information on the most common inhaled allergens:

- Pollen
- Mold
- Dust mites
- Animal dander

Food

Any food can cause an allergic reaction in people of all ages. However, the foods that most commonly cause food allergies include peanuts, wheat, tree nuts, fish, shellfish, eggs, milk, and soy. Symptoms of food allergy can include skin rashes, stomach cramps, nausea, vomiting, diarrhea, or blood in the stool (rarely in very young infants). Many food allergens can cause anaphylaxis, a life-threatening condition that requires immediate medical attention. Food allergy is often confused with food intolerance and other conditions, which are not immune system reactions but may have similar gastrointestinal symptoms.

Insect stings

Insect stings usually cause localized pain and swelling in all people. In people allergic to insect stings, however, they can also cause allergic reactions, including anaphylaxis. An allergic reaction to insect sting venom sometimes happens with stunning swiftness because the allergen is injected directly into the bloodstream.

Medications

Allergies to medicines may produce symptoms throughout the body. The reactions might be severe, including anaphylaxis. Often, though,

these allergies produce symptoms that are quite mild. When medications are injected, the allergic reactions are more likely to appear quickly[7].

Latex

Latex and additives used in the processing of latex can cause an allergic reaction. This has become a growing problem, particularly in the healthcare community, due to the increased use of latex to protect against contagious diseases. For people allergic to latex, repeated exposure can lead to anaphylaxis.

Poison ivy, oak, and sumac

Poison ivy, oak, and sumac are found throughout the United States. These plants have oil on their surface called urushiol. Very small amounts of this oil can cause allergic contact dermatitis, an itchy and blistery rash. This is a classic example of an allergy that does not need antibodies to cause a reaction.

Specific tests

Allergy testing can let you know for certain which allergens are affecting you. Testing may reveal allergens that you didn't even realize were causing you problems. Furthermore, testing is necessary if you wish to start immunotherapy (allergy shots).The allergist will ask questions about your medical history to determine whether allergies run in your family.

Skin prick or scratch test

When most people go to the allergist for the first time, they want to know right away -- "What am I allergic to?" Fortunately, skin testing can usually be done on your first visit, and you may get immediate answers to your questions. However, some medications may affect the accuracy of the test, such as antihistamines and antidepressants. If you are taking any prescription medications, ask your primary care physician and allergist how to prepare for the allergy tests. The skin prick or scratch test is the most common, reliable test for most allergies. The procedure is fairly painless. A small needle or plastic device is used to lightly prick or scratch your back or forearm with a tiny amount of allergen. After 15 - 20 minutes, your allergist will be able to interpret the results by examining each spot where allergens were scratched or pricked into your skin. The spots where you are allergic will become red and swollen, and the others will remain normal.

Fig:10 Skin Test

Intradermal Test

Intradermal testing is done on the patient's upper arms. This may be done for one of the following reasons:

1. No evidence of allergy appeared with prick tests.

2. Some evidence of allergy appeared with prick tests but further evaluation is necessary.

The intradermal test is typically done when the skin prick or scratch test results are negative. It is similar to the prick or scratch test but involves injecting a small amount of allergen under the skin using a needle. The test is also more sensitive, exposing the skin to more allergen than the prick or scratch test.

Fig:11 Intradermal Test

Reactions to skin testing should clear up quickly. Because skin testing involves the injection of allergens under the skin, there is a small risk of anaphylaxis. For this reason, allergy skin testing should only be performed in a medical setting, with access to emergency treatment.

Blood Test

The blood test or RAST (radio allegro sorbent) test measures the levels of the allergy antibody IgE to a specific allergen that is produced when your blood is mixed with a series of allergens in a laboratory. If you are allergic to a substance, the IgE levels against that substance are usually high. The blood test may be used if you have existing skin problems like eczema, if you're on medications that are long-acting or you cannot stop taking,

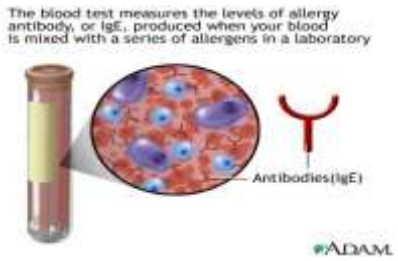


Fig:12 Blood Test

Challenge Test

To find out whether you have an allergy, if your allergist is not certain after testing your skin or blood, you may need a challenge test. There are two types of challenge test: open and blinded. In an open challenge, you gradually swallow increasing amounts of a suspected allergen while you are monitored for allergy symptoms. In a blinded challenge, you swallow a very small amount of the suspected allergen (such as milk or antibiotic), usually in a capsule. Real capsules may are alternated with placebo capsules. Due to the risk of a severe allergic reaction like anaphylaxis, challenge tests are done in a clinical setting and are only performed when absolutely necessary.

Elisa Test

ELISA is an abbreviation for "enzyme-linked immunosorbent assay. ELISA tests are widely utilized to detect substances that have antigenic properties, primarily proteins (as opposed to small molecules and ions such as glucose and potassium). The substances detected by ELISA tests include hormones, bacterial antigens and antibodies. There are variations of the ELISA test, but the most basic type consists of an antibody attached to a solid surface. This antibody has affinity for (will latch on to) the substance of interest, for example, human chorionic gonadotropin (HCG), the commonly measured protein which indicates pregnancy. A mixture of purified HCG linked (coupled) to an enzyme and the test sample (blood, urine, etc) are added to the test system. If no HCG is present in the test sample, then only HCG with linked enzyme will bind. The more HCG which is present in the test sample, the less enzyme linked HCG will bind. The substance the enzyme acts on is then added, and the amount of product measured in some way, such as a change in color of the solution.

ELISA tests are generally relatively accurate tests. They are considered highly sensitive and specific and compare favourably with other

methods used to detect substances in the body, such as radio immune assay (RIA) tests. They have the added advantages of not needing radioisotopes (radioactive substances) or a costly radiation counter (a radiation-counting apparatus).

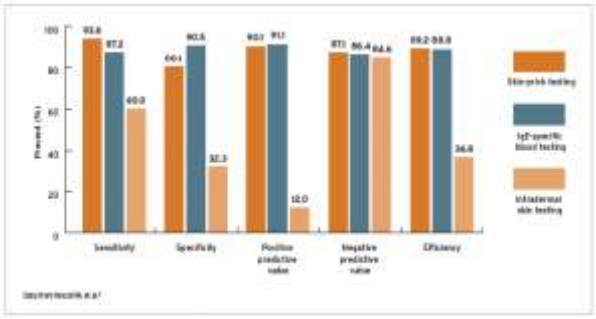


Fig:1 Comparison Allergy Testing Modalities

Immunopathology

Immunity (derived from *immunitas*: Latin for exemption from civic duties and prosecution) means protection from disease and especially infectious disease. Cells and molecules involved in such protection constitute the immune system and the response to introduction of a foreign agent is known as the immune response. Not all immune responses protect from disease; some foreign agents, such as the allergens found in house dust mite, cat dander or rye grass pollen, cause disease as a consequence of inducing an immune response. Likewise some individuals mount immune responses to their own tissues as if they were foreign agents.

Innate and Adaptive Immunity

The normal individual has two levels of defence against foreign agents. The first type is present in neonatal animals and in invertebrate's namely natural or innate immunity. This type of immunity is sometimes referred to as non-specific but broadly specific would be a better description. The second type of immunity is adaptive or acquired immunity and is confined to vertebrates.

Innate (or natural) immunity

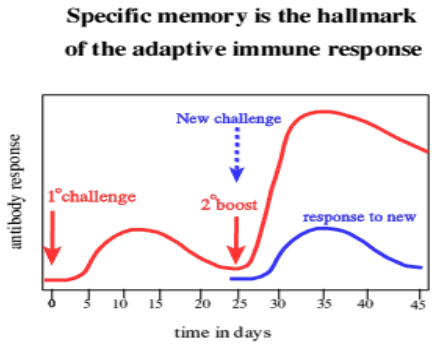
This is made up of several components.

- **Physical barriers are the first line of defence against infection.** The skin and mucous membranes provide a continuous surface which must be breached and back this up with mechanical protection through cilia and mucous.
- **Physiological factors** such as pH, temperature and oxygen tension limit microbial growth. The acid environment of the stomach combined with microbial competition from the commensal flora inhibits gut infection.
- **Protein secretions** into external body fluids such as lysozyme also help resist invasion. Soluble factors within the body such as **complement**, **interferons** and collectins and other "broadly specific" molecules such as C-reactive protein are of considerable importance in protection against infection.
- **Phagocytic cells** are critical in the defence against bacterial and simple eukaryotic pathogens. Macrophages and Polymorphonuclear leucocytes (PMN) can recognise bacterial and yeast cell walls through broadly specific receptors (usually for carbohydrate structures) and this recognition is greatly enhanced by activated complement (opsonin) [as well as by specific antibody.].

Adaptive immunity

The second level of defence increases in strength and effectiveness with each encounter. The foreign agent is recognised in a specific manner and the immune system acquires memory towards it.

(Review Article)



The first encounter with an antigen is known as the primary response. Re-encounter with the same antigen causes a secondary response that is more rapid and powerful.

Acquired immunity is a useful evolutionary adaptation because it improves the efficacy of the innate immune response by focusing the response to the site of invasion/infection as well as providing additional effector mechanisms that are unique to lymphocytes. The difference between innate and acquired immunity lies in the antigen specificity of lymphocytes. This property is conferred upon lymphocytes by the expression of cell surface receptors that recognise discrete parts of the antigen known as antigenic epitopes. The cell surface receptor of B lymphocytes, derived from Bone marrow in mammals or the Bursa of fabricius in chickens, is animmunoglobulin molecule which, when secreted by the B cell, is known as an antibody. Evolution in mammals has led to expansion of the antibody gene pool and a mechanism for generating a vast number of antibodies with a wide range of different specificities. This large repertoire of different antibody specificities arms the immune system to respond to practically all of the potential antigens nature can devise.

Types of Acquired Immunity

There are four types of specific resistance or acquired immunity that are generally recognized. These are: (i) naturally acquired active immunity, (ii) naturally acquired passive immunity, (iii) artificially acquired active immunity and (iv) artificially acquired passive immunity

Allergy Treatment and Precautions

Doctors use four general approaches to help people with allergies: advise them on ways to avoid the allergen as much as possible, prescribe or recommend medication to relieve symptoms, give a long-term series of allergy shots (immunotherapy), and provide ongoing education and communication. Although there is no cure for allergies, one of these strategies -- or a combination of them -- can usually provide relief from allergy symptoms.

Fig:2 Allergy Treatment and Precautions

Your first step towards feeling better on a daily basis is avoiding the things that cause your allergic reactions. Once you have been tested and you know what you're allergic to, there are specific steps to take.

Avoid indoor allergens and irritants

Many people don't realize that the air we breathe inside our own homes can be laden with airborne allergens and irritants. Here is a list of the most common culprits and ways to minimize them:

Pollen -- Stay indoors on days with high pollen levels. If you need to be outside for a while,

consider taking a shower to wash your face and hair after coming indoors. Change your clothes and wash them, and don't dry them on an outdoor clothesline. Keep doors and windows closed, and use the air conditioner if you can. (This applies while you're riding in a car as well.) Obviously, pollen is impossible to avoid outdoors, but you can minimize some of the exposure indoors.

Dust mites -- Encase mattresses, box springs, and pillows with mite-proof covers. Wash bedding once a week in hot water. Replace upholstered furniture with wooden, leather, or vinyl alternatives. Try to keep the indoor humidity level lower than 50%. Remove clutter and stuffed animals from the bedroom. Wipe dust with a damp cloth and vacuum with a high efficiency particulate air (HEPA) filter weekly. Replace wall-to-wall carpet with hardwood or other flooring -- though costly, this can significantly reduce the dust mite populations in your home.

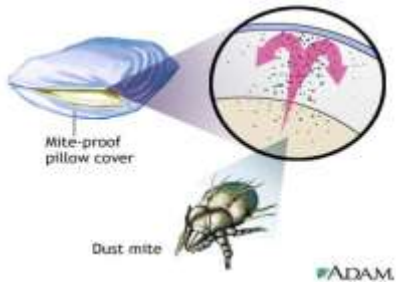


Fig:3 Indoor Allergen and Irritants

Mold spores -- Try to keep the indoor humidity less than 50%. Keep sinks and tubs dry and clean, and fix leaky pipes. Clean the refrigerator tray when necessary. Use an exhaust fan in the bathroom while showering. Avoid putting damp clothes into a basket or hamper. Mold spores can grow in any area of the house that has been damaged by water.

Pet dander -- One of the most important first steps you should try is keeping your pet off beds and linens; in fact, out of the bedroom entirely. Since you lie in bed all night long, you definitely don't want allergens accumulating on your bedding. Try to keep pets off upholstered furniture and carpets as well. Some allergists recommend washing your pet once a week to minimize the amount of allergen given off, but that may be impractical. Consider installing a HEPA filter if you have a central air conditioning system to remove airborne pet allergen. Vacuum cleaners with HEPA filters may help. If these measures don't help and your symptoms are greatly impacting your life, you may have to consider immunotherapy or finding your pet a new home.

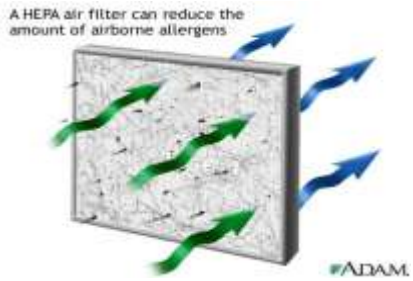


Fig:4 Hepa Filter

Cockroaches -- Wipe off counters in the kitchen, and avoid leaving dirty dishes in the sink. Keep food in closed containers. Take out the trash regularly, including bags, newspapers, and cardboard boxes. Use roach traps.

Tobacco or wood smoke -- Don't allow smoking in the house or car. Encourage family members and friends to stop smoking around you. Avoid using fireplaces. If you need to burn wood, use an air-tight wood burning stove.

(Review Article)

Cleaning agents

Avoid using cleaning agents and sprays (such as bleach) that can irritate the airways of someone with allergies and asthma.

Allergy Medication

If you are still having symptoms despite your efforts to avoid allergens, you might explore medication options. Regardless of which medications you select, read the product labels and know the side effects. The following list includes the most common allergy treatments (both over-the-counter and prescription) and the specific allergic conditions they treat. Particularly when treating children for allergies, it is wise to consult with your health care provider. Some of the medications are not as effective in children, and some of the medications can affect behaviour and sleep, as well as cause more serious side effects.

Fig:5 Allergy Medication

Antihistamines

As the name implies, antihistamines counter the effects of histamine released during an allergic reaction. They are widely used to treat many allergy-related conditions. They are often combined with decongestants and are available in a variety of over-the-counter formulas (such as Advil Allergy Sinus, Alavert Allergy and Sinus, Benadryl, Chlor-Trimeton, Claritin, Contac, Dimetapp, Robitussin Cough and Allergy, Triaminic Cold and Allergy, and Tylenol Allergy) and by prescription (such as Allegra, Clarinex, and Zyrtec). You should always ask your pharmacist if your antihistamine also contains a decongestant, especially any you give to children. Some antihistamines may cause drowsiness and slowed reaction time. Others do not. Antihistamine nasal sprays are also available to treat allergic rhinitis (such as Astelin). Antihistamine eye drops may also be used for quick relief of itchy eyes associated with allergies (such as Patanol).

Leukotriene blockers

Leukotrienes are another substance released in the body that trigger allergic symptoms such as a stuffy or runny nose, sneezing, itchy eyes, postnasal drip, or wheezing. Montelukast sodium (Singulair) is a prescription medicine that can prevent symptoms by blocking leukotrienes. It is used in adults and in children as young as two years. It is also used to treat asthma.

Decongestants

People who experience nasal congestion (stuffy nose) due to allergies or sinusitis sometimes consider oral or nasal spray decongestants for relief. Decongestants are also included in eye drops to decrease redness caused by conjunctivitis. They work by constricting blood vessels and reducing swelling. Be careful when using some nasal spray decongestants. If you use them for a prolonged period (longer than 3 - 4 days), you may experience a "rebound" effect, where nasal congestion symptoms return. Concerns have been raised about oral decongestants and their side effects (especially for children) and potential for misuse. They are now available behind the counter. Ask your pharmacist; you should ask your child's pediatrician about decongestant use in children.[7]

(Review Article)

Corticosteroids

These anti-inflammatory agents are used to treat the itching and swelling associated with a variety of allergic disorders. The most commonly used forms are corticosteroid nasal sprays for allergic rhinitis and sinusitis (such as Flonase, Nasalide, Nasocort, Nasonex, Rhinocort), over-the-counter topical corticosteroid creams for hives, dermatitis, and insect sting reactions, and inhaled corticosteroids for asthma. Oral or injected corticosteroids are used less frequently for more severe cases of asthma, dermatitis, or other allergic reactions.

Cromolyn Sodium/Nedocromil Sodium

These are another type of anti-inflammatory medication. Cromolyn sodium nasal spray can be used to treat and sometimes prevent allergic rhinitis. It works by preventing the release of histamine from mast cells. Cromolyn nasal spray is available over the counter and is gentle and effective. It generally takes a few days to start working. Eye drop versions are available for itchy, bloodshot eyes. Inhaled nedocromil sodium is used to treat inflammation due to asthma, which can be exacerbated by allergies. It is more often used in children.

Histamine

Histamine meaning "tissue a mine" (histos-tissue) is almost ubiquitously present in animal tissue and in certain peanuts eg. *Stinining nettu*., its pharmacology was studied in detail by Dale in the beginning of the present century when close parallelism was noted between its actions and the manifestations of certain allergic reactions. It was implicated as a mediator of hypersensitivity phenomena and tissue injury reactions. It is now known to play important physiological roles. Histamine is present mostly within storage granules of mast cells. Tissues rich in histamine are skin, gastric and intestinal mucosa. Lungs, liver and placenta. Nonmast cell histamine occurs in brain, epidermis, gastric mucosa and growing regions. Turnover of mast cell histamine is slow, while that of nonmast cell histamine is fast. Histamine is also present in blood, most body secretions, venoms and pathological fluids.

Synthesis, storage and destruction

Histamin is β imidazolylethylamine. It is synthesized locally from the amino acid histidine and degraded rapidly by oxidation and methylation (Fig:19). In mast cells, histamine (positively charged) is held by an acidic protein and heparin (negatively charged) within intracellular granules. When granules are extruded by exocytosis Na^+ ions is e.c.f. exchange with histamine to release it free. Increase in intracellular cAMP inhibits release. Histamine is inaction orally because liver degrades all histamine that is absorbed from the intestines.

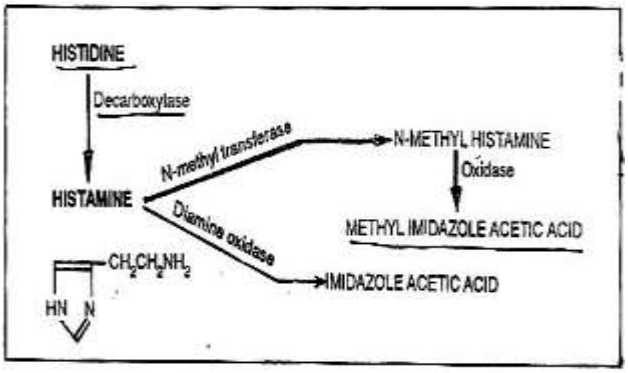


Fig: 6 Synthesis, Storage and Destruction of Histamine

Histamine receptors

Analogous to adrenergic α receptors, histaminergic receptors were classified by Asch and Schild (1996) into H_1 and H_2: those blocked by then available anthistamines were labelled

H_1. Sir James Black (1972) developed the first H_2 blocker burimamide and confirmed this classification. Both H_1 and H_2 receptors have now been cloned. A third H_3 receptor, which serves primarily as an autoreceptor controlling histamine release from neurons in brain was postulated by Schwartz) and confirmed by Arang in 1987. No H_3 selective agonist or antagonist has so far been developed for clinical use.

Pharmacological Actions

Blood vessels

Histamine caused marked dilation of smaller blood vessels including arterioles, capillaries and venules. On subcutaneous injection, especially in the blush area, heat, increased heart rate and cardiac output, with little or no fall in BP are produced. Rapid i.v. injection causes fall in BP which has an early short lasting H_1 and a slow but more action is seen, in this way it shows action on blood vessel. Persistent H_2 component, with low does only the H_1 component is manifest since H_1 receptors have higher affinity. Fall in BP due to large doses in completely blocked only by a combination of H_1 and H_2 antagonists. Dilatation of cranial vessels causes pulsatile headache.

Like acetylcholine and many other autacoids, vasodilatation caused by histamine is partly (H_1 component) indirect, mediated through 'endothelium dependent relaxing factor' (EDRF): the receptor being located on the endothelial cells, H_2 receptors mediation vasodilatation is located directly on vascular smooth muscles. Larger arteries and veins are constricted by histamine: mediated by H_1 receptor on vascular smooth muscle. Histamine also causes increased capillary permeability due to separation of endothelial cells- exudation of plasma. This is primarily a H_1 response Injected intradermally, it elicits the triple response consisting of:

Red spot: due to intense capillary dilatation

Wheal: due to exudation of fluid from capillaries and venules

Flare: i.e. redness in the surrounding area due to arteriolar dilatation mediated by axon reflex.

Heart

Direct effects of histamine of in situ heart are not prominent, but the isolated heart, especially of guinea pig, is markedly stimulated-rate as well as force of contraction is increased. These are primarily H_2 response but a H_1 mediated negative dromotropic (slowing of A-V conduction) effect has also been demonstrated.

Visceral smooth muscle

Histamine causes bronchoconstriction; guinea pigs and patients of asthma are highly sensitive. Large doses cause abdominal cramps and colic by increasing intestinal contraction. Guinea pig uterus is contracted while that or rat is relaxed human uterus is not much affected as are most other visceral smooth muscles. Smooth muscle contraction is a H_1 response. In few instances H_2 mediated relaxation is also seen, e.g. bronchial muscle of sheep.

Glands

Histamine causes a marked increase in gastric secretion-primarily of acid but of pepsin. This is a direct action excreted on paretal cells through H_2 receptors and is mediated by increase cAMP generation, which in turn activates the membrane proton pump (H^+K^+ ATPase)

Histamine can increase other secretions also, but the effect is hardly discernable.

Sensory nerve endings

Itching occurs when histamine is injected i.v. or intra-cutaneously. Higher concentration injected more deeply cause pain. These are reflection of the capacity of histamine to stimulate nerve endings.

Autonomic ganglia and adrenal medulla

These are stimulated and release of Adroccurs. This can cause a secondary rise in BP

CNS

Histamine does not penetrate blood brain barrier – no central effects are seen on i.v. injection. However, intracerebroventricular administration produces rise in BP, cardiac stimulate, behavioural arousal, hypothermia, vomiting and ADH release. These effects are mediated through both H_1 and H_2 receptors.

Pathophysiological Roles

Gastric secretion

Histamine has dominant physiological role in mediating secretion of HCl in the stomach. Nonmast cell histamine occurs in gastric mucosa, possibly in cells called 'histaminocytes' situated close to the parietal cells and has high turnover rate. It is released locally under the influence of all stimuli that evoke gastric secretion (feeding, vagal stimulation, cholinergic drugs and gastrin). H_2 blockers not only block acid secretion induced by histamine but also markedly diminish that in response to Ach and gastrin. By a mutually synergistic interaction the there secretagogues amplify responses to each other with histamine playing the dominant role. As such, antimuscarinic drug dampen the response to histamine and gastrin also. All there secretagogues activate same proton pump (H^+ K^+ ATPase) in parietal cell membrane, but through their own receptors.

Uses

Histaime has not therapeutic use. However, there are some diagnostic uses. Test of acid secreting capacity of stomach; Now pentagastrin (a synthetic gastrin analogue) is preferred-it produces few side effects, Injected s.c. 6µ/kg pentagastrin produces increased gastric secretion lasting an hour so.

Pheochromocytoma: Histamine causes rise in BP in these patients (by releasing CAs from the tumour) instead of the usual fall. This is dangerous test: catastrophic rise in BP can occur phentolamine must be at hand.

To test bronchial hyper reactivity in asthmatics.

Betahistine

It is an orally active, somewhat H_1 selective histamine analogue. It has been used to control vertigo in patients of Meniere's disease: possible acts by causing vasodilatation in the internal ear. It s contraindicated in asthmatics and ulcer patients. VERTIN 8 mg tab., ½ to 1 tabl QID.

Histamine Releasers

A variety of mechanical, chemical and immunological stimuli are capable of releasing histamine from mast cells

1. Tissue damage: trauma, stings and venoms, proteolytic enzymes, phophlipase
2. Antigen: antibody reaction involving IgE antibodies.

3. Polymers like dextran, polyvinyl pyrrolidone (PVP)
4. Some basic drugs-tubocuraine, morphine, atropine, stilbamidine, polymyxin B, vancomycin and even some antihistaminics directly release histamine without an immunological reaction.

Surface acting agents like Tween 80, compound 48/80 etc. the primary action of these substances is release of histamine from mast cells, therefore they are called histamine laboratory. They produce an 'anaphylactoid' reaction-itching and burning sensation , flushing, urticaria, fall in BP, tachycardia, headache, colic and asthma, Most of these symptoms are controlled by a H_1 antihistminic, better still if H_2 blocker is given together.

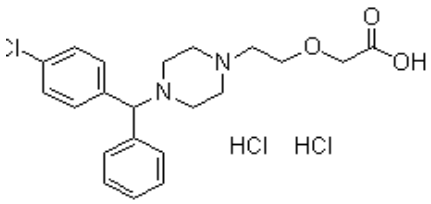
PHARMACOLOGY OF NEWER DRUGS

CETIRIZINE HYDROCHLORIDE

Brand Name(S) Zyrtec

Synonym - 2-(2-{4-[(4-Chlorophenyl)(phenyl)-methyl]piperazino}ethoxy)acetic acid dihydrochloride

Molecular Structure-



Mechanism of Action

Cetirizine, a human metabolite of hydroxyzine, is characterized by its high selectivity for the H1 receptor site and its reliable and consistent inhibition of histamine-induced allergic reactions. It also blocks eosinophil infiltration to the site of allergen-induced cutaneous reactions. Cetirizine has proved effective in the treatment of seasonal and perennial allergic rhinitis and urticaria. It is excreted primarily by renal mechanisms. It is well tolerated by elderly patients. Cetirizine has a low rate of penetration of the blood-brain barrier, and it has minimal central nervous system impairment.[8]

Uses

Cetirizine, an antihistamine, is used to relieve hay fever and seasonal allergy symptoms, including runny nose; sneezing; and red, itchy, tearing eyes. It also may be used to treat itching and hives that result from certain skin conditions. This medication is sometimes prescribed for other uses; ask your doctor or pharmacist for more information.

Side Effects

Although side effects from cetirizine are not common, they can occur. Tell your doctor if any of these symptoms are severe or do not go away:

- dry mouth, nose, and throat
- drowsiness
- dizziness
- upset stomach
- If you experience any of the following symptoms, call your doctor immediately
- fast or irregular heartbeat
- difficulty urinating

LEVOCETRIZINE DIHYDROCHLORIDE

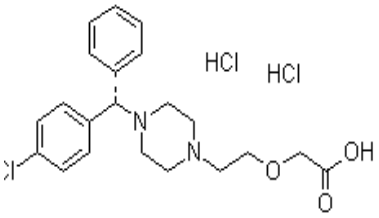
Chemical Name: (R)-[2-[4-[(4-chlorophenyl) phenylmethyl]-1-piperazinyl] ethoxy] acetic acid dihydrochloride. Levocetirizine dihydrochloride, the active component of XYZAL tablets and oral solution, is an orally active H1-receptor antagonist. Levocetirizine dihydrochloride is the R enantiomer of cetirizine hydrochloride, a

racemic compound with antihistaminic properties.

Empirical Formula: $C_{21}H_{25}ClN_2O_3$•2HCl.

Molecular Weight: 461.82

Molecular Structure:



Mechanism of Action

Selective peripheral H1 receptor antagonist. The increased polarity of Levocetrizine may decrease distribution of the drug into the CNS, resulting in reduced potential for adverse CNS effects. Tolerance to Levocetrizine does not occurs. Does not cross blood brain barrier. Rapidly absorbed from GIT. Peak Plasma concentration and AUCs of Levocetrizine is increased in patient with renal and hepatic impairment, which needs reduction of dose.

Dose

Adult: 5 mg OD orally. Children of 6 years age or above, 5 mg as adult.

Children below 6 years: No adjusted dose is yet possible.

Elderly: Adjust dose on the basis of renal function.

Patients with renal impairment: Dose adjusting according to renal function.

Pregnancy: Use with caution.

Use

This medication is an antihistamine that treats symptoms such as itching, runny nose, watery eyes, and sneezing from "hay fever" and other allergies. It is also used to relieve itching from hives. Special use in PERSISTENT ALLERGIC RHINITIS. This medication works by blocking a certain natural substance (histamine) that your body makes during an allergic reaction.

Side effect

- Headache,
- somnolence,
- dry mouth,
- mild drowsiness
- GI disturbances.

CONCLUSION

Allergy is characterized by local or systemic response to outside allergens such as dust, pollen or certain foods. Local symptoms are observed like allergic rhinitis, conjunctival, skin rasher and systemic symptoms like dyspnoea, bronchoconstriction, oedema, hypoknision, Coma and some time death also.

Diagnosis of allergy is based on the medical history and physical examination. In case of diagnostic uncertainty, testing for specific antigens can be useful.

Histamine is the main mediator for allergy. Histamine is present mostly within storage granules of mast cells. Tissues mucosa, lungs, liver and placements. It is also present in blood, body secretions etc. Effect of Histamine is mediated through Histamine receptors H_1 H_2 and H_3. These receptors are situated in various parts.

There are various drugs with are used or antihistamines. Diphenhydromins, Promethazene, pheneramine, Antazolene, chlorphesiramine, Mepyramine. Terfenadine, Astemizole, loratadine, Azelastine etc. There are some new drugs which are introduced is levocetrizene, Desloratadine, Fexofandine, Azdasaine, These new drugs are covered in details in the dissertation work.

REFERENCES:

1. Ash ASF, and Schild HO, Receptors mediating some actions of histamine. Br. J.Pharmacol. 1966, 27, 427-439.

2. Cohen B, and deJong JMBV, Meclizine and placebo in treating vertigo of vestibular origin. Relative efficacy in a double-blind sstudy. Arch. Neurol. 1972, 27,129-135.

3. Date HM, and Lawidlaw PP, The physiological action of β-imidazolylethylamine. J.Physiol. (Lond). 1910, 41,318-344.

4. Farmer SG, Burch RM, Meeker SA, and Wilkins DE, Evidence for a pulmonary B bradykinin receptor Mol. Pharmacol. 1989, 36, 1-8.

5. Graybiel A, Wood CD, Kneptorn J, Hoche J, and Perkins GF, Human assay of antimotion sickness drugs. Aviat. Space Environ. Med. 758, 46, 1107-1118.

6. Jacob R, Merrit JE, Hallam TJ, and Rink TJ, Repetitive spikes in cytoplasmic calcium evoked by his tamine in human endothelial cells. Nature. 1988, 335, 40-45.

7. Takagaki Y, Kitamura N, and Nakanishi S, sequence analysis of cDNAs for human high molecular weight prekinioogens. J. Biol. Chem. 1985, 260, 8601-8609.

8. Lewis T, The blood vessels of the Human skin and Their Responses. Shaw & Sons, Ltd. London, 1927.